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Formulation and Evaluation of Topical Herbal Cream for Cellulitis

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ABSTRACT:

Staphylococcus aureus (S. aureus), a bacterium that causes skin infection as a result of skin colonization; it is becoming increasingly resistant to many commonly used for antibiotics. TermeneliaBellerica or Baheda, traditionally used for the treatment of inflammation and infection, in extract form has been shown to exhibited anti-bacterial activity against various bacteria. This study aims to examine the anti-bacterial properties of T.bellerica towards S.aureus and formulate T.Bellerica into cream to determine its anti-bacterial properties. Different concentrations (5%, 25%, 50%, 75% and 100%) of aqueous extract of and cream containing T.Bellerica were used in the disc diffusion method for determination of antibacterial activity towards S.aureus. Microbiological pre- and post-testing were carried out for both extract and cream formulations to determine their anti-bacterial properties. Both extract and cream containing T.Bellerica showed good anti-bacterial properties against S.aureus. The anti-bacterial activities were proportional to the concentration of extract alone and in the cream. All cream formulations showed satisfactory physical properties with smooth texture, emollient, non-greasy and easy to remove with water. It is concluded that T.Bellerica has potential to be developed as a cream for skin infections caused by S.aureus. The zone of inhibition is seen on the cup plate method of extract with conc. of 1000, 1500, 2000 µg/ml and the reading is compared with the standard. The evaluation is done on the formulation.

KEY WORDS: Cellulitis, Termenillia bellerica, Cream formulation.

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INTRODUCTION:

There are two group of drug products that are topically administered through the skin. The category includes products that are applied for local action. In this case, the active ingredient(s) stay on the skin surface or penetrate through the epidermal layers and may reach the dermis, but are not absorbed into the blood circulation. This group is usually defined as topical drug delivery system. The other category is termed transdermal drug delivery or transdermal patches that are applied for their systemic effect. The active ingredients are delivered into the general blood circulation to produce a therapeutic response by traversing through the different layers of the skin. Cellulitis is an chronic condition that is been handled early in any medical setting, from primary to tertiary cares. All age is been affected, suddenly in healthy patients also, there is several local and general predisposing conditions that might favor the occurrence. Acute complications are fortunately rare, but life-threatening. Long-term complications are recurrences and persistent lymphedema, which further favor aggravation. The plant Terminaliabelericabelongs to family CombretaceaeGlucoside (bellericanin), Gallo-tannic acid, Coloring matter,

resins and a greenish yellow oil. Ellargic acid, gallic acid, lignans(termilignan and thannilignan), 7-hydroxy 3'4' (methylene dioxy) flavone and anolignan B10. Tannins, ellargic acid, ethyl gallate, galloyl glucose and chebulaginic acid, phenyllemblin, β-sitosterol, mannitol, glucose, fructose and rhamnose.[1, 2]

MATERIALS AND METHOD

Table 1:Materials Used

Sterai Acid	AaturInstruChem
White beeswax	AaturInstruChem
StearylAchohol	Chemdyes
Liquid Paraffin	Suvidhinath laboratory
Propylene Glycol	Qualikems
Triethanolamine	Chemdyes
Methyl Paraben	Oxford laboratory
Propyl Paraben	Chiti-Chem Corporation
Plant Extract	Hindustan Biosynthesis Limited

Method of Preparation[3]

Cream containig extract of TermeniliaBellerica was prepared by o/w type cream formulation as shown in. The oil phase is 1st added then aqueous phase and on cooling cream is been formed. The extract and excipients were mixed through o/w type of the formulation. The excipients are stepwise added on the china dish and on proper mixer with oily phase in aqueous phase the batch are been made. Preliminarily thirteen formulations were designed for screening of excipients. The batches is been made to see the different formulation with the action on the viscosity, PH and spreadibility. Based on the results obtained further experiments were designed by 3^2 factorial to develop optimized formula.

CHARACTERIZATION OF ANTI-BACTERIAL CREAM[4-6]

- **Screeening of plant extract**

From the above selected 6 extract one extract will be selected by seeing the highest zone of inhibition of the extract on S.areus.

- **Physicochemical properties**

All the parameters like color, odour, solubility, pH, ash value, moisture content, extractive value are been seen.

- **Phytochemical Screening**

Test for carbohydrates, alkaloids, glycosides, tannins, flavonoids, steroids, volatile oils.

- **Antibacterial Activity**

The nutrient agar plate is been made, then the plate is been autoclave for sterilization for 30 mim then the plate is removed from the autoclave .The plate is then taken to under laminar air flow ,there the bacteria is incorporated in the plates and put it for solidified.

Then with the borer wells are made the extract concentration is 1000, 1500, 2000 µg/ml is incorporated inside the wells and put it for 30 mim and then this plates is put in the incubator for incubation .Reading taken for 24 hrs,48hrs.

Preformulation studies

Identification confirmatory test for Termenilia Belerica

- **FTIR study**

The identity of the pure TermeniliaBelericasample was studied by scanning the sample in the wave number range 400-4000 cm^{-1} using FTIR spectroscopy by KBr pellet method. The finger print obtained was compared with the reference standard.

- **Drug excipients compatibility study:**

Excipients are integral component of almost all pharmaceutical dosage forms. The successful formulation of a stable and effectual dosage form depends on the cautious selection of the excipients, which are added to make easy administration, promote the steady release and bioavailability of the drug and to protect it from degradation.

The drug and polymer interactions were studied by Fourier transform infrared spectroscopy by potassium bromide (KBr) disc method. In this method, a small amount of drug was mixed with the spectroscopic grade of KBr and triturated for uniform mixing. A thin and transparent pellet was prepared by applying 2000 psi pressure. The prepared pellet was exposed to the IR beam and spectra were recorded at the scanning range of 400-4000 cm^{-1} by using FTIR spectrophotometer.

Method of analysis of Termenilia Belerica

- **Preparation of phosphate buffer**

Place 50 ml of 0.2M KH_2PO_4 in a 200ml of volumetric flask, add specified volume of 0.2M NaOH and then add water to volume upto 1000ml.

- **Determination of absorption maxima (λ_{max})**

The stock solution was prepared by dissolving accurately weighed 10 mg of Termeniliabellericain small amount of phosphate buffer pH 7.4and the volume was made up to 100 ml with the same to obtain a concentration of 100µg/ml.

The stock solution was diluted with phosphate buffer pH 7.4and was scanned for UV spectrum by using Shimadzu UV spectrophotometer.

- **Standard calibration curve of Termenilia Belerica in Buffer**

The stock solution was prepared by dissolving accurately weighed 10 mg of TermeniliaBelerica in small amount of phosphate buffer pH 7.4 and the volume was made up to 100 ml with the same to obtain a concentration of 100 µg/ml.

From the above stock solution (100 µg/ml) aliquots of 10, 30, 50, 70, and 90 ml were transferred to a series of 10 ml volumetric flask and diluted up to the mark with phosphate buffer to obtain concentration of 10, 30, 50, 70, and 90µg/ml. Absorbance was measured spectrophotometrically at λ_{max} of 273 nm against 0.1N HCl using UV spectrophotometer.

Evaluation studies of preparation

- **Anti Cellulitis Activity**

The activity is been checked by the agar well diffusion method. The zone of inhibition is been checked for the activity of extract. The nutrient agar plate is been made, then the plate is been autoclave for sterilization for 30 mim then the plate is removed from the autoclave .The plate is then taken to under laminar air flow ,there the bacteria is incorporated in the plates and put it for solidified.

Then with the borer wells are made the extract concentration is 1000, 1500, 2000 µg/ml is incorporated inside the wells and put it for 30 mim and then this plates is put in the incubator for incubation .Reading taken for 24 hrs,48hrs.

- **pH**

The pH of the formulation was measured using pH meter. The instrument was calibrated using buffer solution of pH 4 and pH 7 by dipping the electrode in it. The pH of the cream was observed. Results were taken in triplicate, average was taken and SD was calculated.

- **Acid value**

Take 10 gram of substance dissolved in accurately weighed 50 ml mixture of equal volume of alcohol and solvent ether, the flask is connected to reflux condenser and slowly heated, until sample is dissolved completely, to this 1 ml of phenolphthalein added and titrated with 0.1 N Naoh, until faintly pink colour appears after shaking for 30 seconds.

Acid value = n * 5.61 / w

Where,

n = the number of ml of Naoh required

w = the weight of substance

- **Saponification Value**

Introduce about 2 gm of substance refluxed with 25 ml of 0.5 N alcoholic KOH for 30 minutes, to this 1 ml of phenolphthalein added and titrated immediately, with 0.5 N HCL.

Saponification value = (b – a) * 28.05 / w

Where,

a = volume of titrant in ml

b = volume of titrate in ml

w = weight of substance in gm

- **Spreadibility**

Spreadability of formulations will be determined by an apparatus, which consist of a wooden block, with a fixed glass slide and movable glass slide with one end tied to weight pan rolled on the pulley, which was in horizontal level with fixed slide.

Spreadability (S) = M * L / T

Where,

M = weight tied to upper slide

L = length of glass slide

T = time taken to separate the slide completely from each other

- **Viscocity**

The viscosity was measured to determine rheological properties of formulation. The viscosity of cream was measured by using Brookfield Rheometer viscometer with spindle no.96 at 10 RPM and 30±2 ˚C. Results were taken in triplicate, average was taken and SD was calculated.

- **In-vitro permeation study**

The drug content of drug loaded cream was measured using UV visible spectroscopic method. The aliquots of cream formulation were prepared using Phosphate buffer. The samples were measured at λmax = 271 nm

using UV-VIS spectroscopic method. Results were taken in triplicate, average was taken and SD was calculated.

➢ **In vitro drug release studies**

The in vitro diffusion study of the cream was carried out in modifiedDiffusion cell using cellophane membrane. The membrane was soaked in phosphate buffer pH 7.4 for overnight was clamped carefully to one end of the hollow glass tube of dialysis cell (2.3 cm diameter; 4-16 cm2 area). Then cream was spread uniformly on the dialysis membrane. 80 ml of phosphate buffer was taken in a beaker, which was used as receptor compartment. The donor compartment was kept in contact with receptor compartment. This whole assembly was kept on a magnetic stirrer and the solution on the receptor side was stirred continuously using a magnetic bead and temperature of the cell was maintained at 37±2 °C. Sample (5 ml) was withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. The Samples were analyzedspectrophotometrically at λmax = 271 nm and the cumulative percent drug release were calculated. Average was taken and SD was calculated.

➢ **Skin irritation study**

The protocol of preclinical study on healthy rabbits was approved by Institutional Animal Ethical Committee, Pioneer Pharmacy Degree College, Vadodara, Gujarat, India (OGECT/PPDC/IAEC/2016/12/13). Experiments were conducted according to the guidelines of "Committee for the Purpose of Control and Supervision of Experiment on Animals" (CPCSEA).

The extract of Termeniliabellerica loaded cream formulation causes skin irritation or not will be checked.Albino rabbits (either sex) will be used in this experiment. They will be housed in cage and maintained on a 12 hours light/dark cycle at RT and RH of 45–55%. They will be acclimatized to laboratory conditions for 1 week prior to application. Animals will be divided into two groups (n = 2).

Group I- Control rabbit without treatment

Group II- First site for Termeniliabellerica loaded cream formulation and second site for blank cream base (without extract) applied rabbits

Albino rabbits(either sex) weighing 1.5 – 2.5 kg will be fasted for 12 h prior to the experiments but allowed free access to water. The hair from back of rabbit will be shaved off and cream will be applied topically.

- Dose :- 0.5 g cream
- Group I will be kept without any treatment under controlled conditions.
- Group II will be treated with Termeniliabellerica loaded cream formulation and blank cream base (without extract) on two different sites.
- The observations for erythema and edema were made after 0, 24, 48 and 72 hours and Primary Irritation Index (PII) will be calculated.

➢ **HPLC of Extract**

10 mg of herbal powder extract was accurately weighed containing 6-14 % of Termeniliabellerica and dissolved into 10 ml mobile phase ACN: Water (92:8) (1000 µg/ml). The solution was sonicate for 10 min and filtered through 0.45 µ whatmann filter paper. Further 0.1 ml of solution was withdrawn from above solution and diluted to 10 ml with mobile phase ACN: Water (92:8) (10 µg/ml). Parameters of obtained solution were noted at 271 nm.

➢ **Stability studies**

Stability studies were performed to check the effect of environmental condition or storage conditions on formulation. However the studies will take a longer time and hence it would be convenient to carry out the accelerated stability studies where the product is stored under extreme condition of temperature. To assess the drug and formulation stability, this stability study is done. The optimized formulation is sealed in the aluminum packing and various replicates were kept in humidity chamber maintained at 40ºC and 75%RH FOR 30 days. The sample is analayzed for the physical changes, %drug content, cream properties and in vitro diffusion study.

RESULTS AND DISCUSSION

➢ **FTIR study**

The FTIR spectrum of pure Termenilliabellerica is shown in Figure 5.1. The FTIR spectrum of Termenilliabellerica showed characteristic peaks at 2951, 1306 and 1265 cm^{-1} due to presence of –CH stretching, may be confirmed to the presence of –C=N bond and C-S bond respectively.Asharp peak occurred at 1564 and 1458 cm^{-1} due to –C=C stretching vibration.

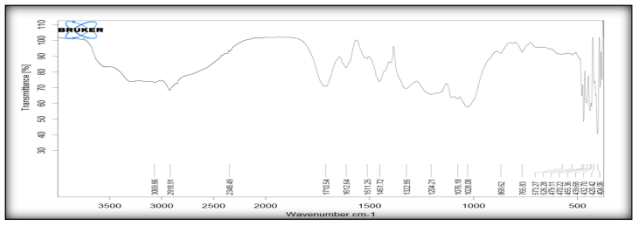


Figure 1: FTIR spectrum of Termenillia bellerica

➢ **Drug excipients compatibility study**[7]

The pure TermenilliaBellerica and its mixture with Steraric acid and Stearyl Alcohol was mixed separately with IR grade KBr and were scanned over a range of 400-4500 cm^{-1} using FTIR instrument. It was observed that there were no changes in the main peaks of TermenilliaBellerica in the FTIR spectra of a mixture of drug and polymers as well as in the physical mixture of all ingredients used in the formulation of tablets . The FTIR study revealed no physical or chemical interactions of Steraicacid,Stearyl alcohol and white bees wax as well as with any other excipients.

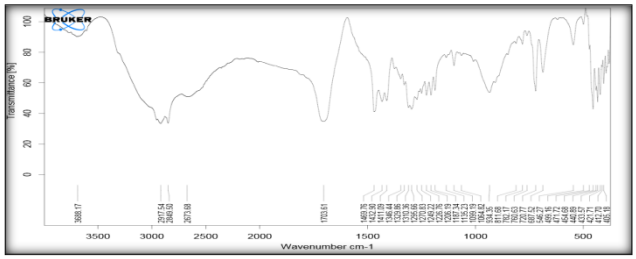


FIGURE2: FTIR SPECTRA OF CREAM FROMULATION

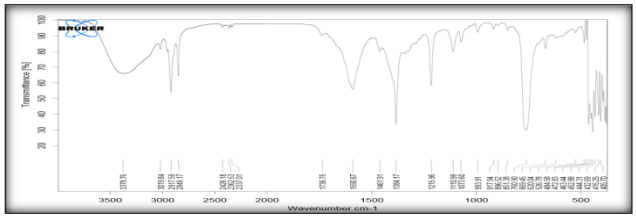


FIGURE 3:FTIR SPECTRA OF STEARYL ALCOHOL

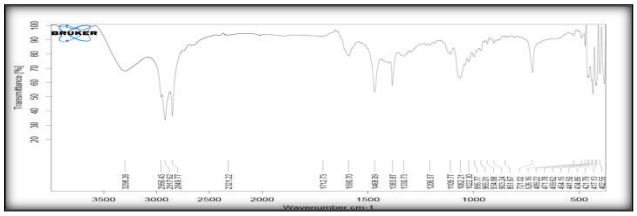


FIGURE4: FTIR SPECTRA OF PHYSICAL MIXTURE

Physicochemical properties

All the parameters like color, odour, solubility, pH, ash value, moisture content, extractive value are been seen.

Table 2: Physicochemical properties of Termenilia bellerica

PARAMATER	% VALUE
Loss on drying	11.0
Total ash	18.0
Water soluble ash	1.83
Acid insoluble ash	11.7
Petroleum ether soluble extractive value	0.9
Ethyl acetate soluble extractive value	2.5
Acetone soluble extractive value	6.1
Aqueous soluble extractive value	20.5

Phytochemical Screening

Test for carbohydrates, alkaloids, glycosides, tannins, flavonoids, steroids, volatile oils.

Table 3 : Phytochemical Screening for Termenilia bellerica

Chemical Test	Test Results
Alkaloids	-
Flavonoids	+
Tannins	+
Cardiac Glycosides	-
Triterpenes	+
Steroids	-
Saponins	-

Formulation Optimization

Table 4: Factors, Factor level and Response

Factors	Factor level used			Response
	-1	**0**	1	
X_1 = amount of Stearyl alcohol	5	7	9	**Y_1=Spreadibilty** **Y_2=Viscosity** **Y_3% Drug release**
X_2 = amount of White beeswax	**3**	**5**	**7**	

TABLE 5: FACTORIAL FOR FORMULATION OF CREAM

Batch	Baheda	White beeswax	Stearyl Alcohol	Steraic Acid	Liquid Paraffin	Propyl Glycol	Triethanolamine	Methy Paraben	Propyl Paraben
0F1	5	3	5	2.5	1	5	2	0.01	0.04
0F2	5	3	7	2.5	1	5	2	0.01	0.04
0F3	5	3	9	2.5	1	5	2	0.01	0.04
0F4	5	5	5	2.5	1	5	2	0.01	0.04
0F5	5	5	7	2.5	1	5	2	0.01	0.04
0F6	5	5	9	2.5	1	5	2	0.01	0.04
0F7	5	7	5	2.5	1	5	2	0.01	0.04
0F8	5	7	7	2.5	1	5	2	0.01	0.04
0F9	5	7	9	2.5	1	5	2	0.01	0.04

Evaluation of Extract with antibiotics

The evaluation of the batches is made is zone of inhibition of the extract first of 24 hrs and 48 hrs compared with the tetracyclin standard

Table 6: Zone of inhibition

	Concentration (µg/ml)	Zone of inhibition (mean ± Standard Deviation) After 24 hr	After 48 hr
Termenilliabelleric aloaded cream	1000	16.3±0.41	18.5±0.3
	1500	17.53±0.53	20.4±0.208
	2000	22.63±0.35	24.13±0.90
Tetaracyclin Cream	1000	18.6±0.21	19.85±0.21
	1500	19.9±0.62	21.3±0.45
	2000	24.2±0.65	26.6±0.72

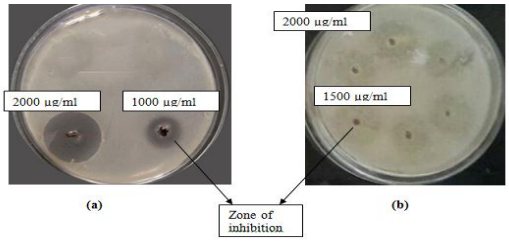


Figure 5: Images of Zone of inhibition of (a)TermenilliaBellerica (b) Tetaracyclin

Minimal inhibitory concentration (MIC)

The minimal inhibitory concentrations were determined as described earlier. Different concentrations of T. bellerica crude extract in nutrient broth were serially diluted in duplicates. Control test tubes did not receive any T. bellenca extract. Later 103 cells of S. aureus in 0.02 ml volume was added into each test tube and incubated at 370 C for 18-24 h. The lowest concentration of drug which inhibited the growth was considered as MIC. The MIC foTermeniliabellerica was found to be 300 µg/ml.

Table 7: Post-compression parameters of preliminary batches

Batch Code	pH	Spreadability (gm.cm/sec)	Viscosity (cps) (100 rpm)	Zone of Inhibition (mm)	% Drug release
0F1	6.7	13.33	1423	19.24	74.24
0F2	6.7	14.55	1523	19.52	78.85
0F3	6.8	15.65	1679	19.2	82.32
0F4	6.7	16.52	1779	18.56	85.36
0F5	6.8	16.45	1813	20.25	84.36
0F6	6.7	17.78	1984	23.32	82.65
0F7	6.8	17	2003	24.45	84.32
0F8	6.8	16.45	1874	24.73	85.61
0F9	6.7	18.45	1895	24.65	83.25

Post-compression evaluation of preliminary trial batches

The batches evaluation is taken on viscosity, pH, Zone of inhibition spreadibility of the cream formulation that is done for first 13 batches of the preparation.

Contour plots and Response surface plots

Contour plots were established between X_1 and X_2 at fixed level of -1, 0 and 1. And they are diagrammatically represented in Figure 9 and 11. By establishment of two dimensional contour plots, the relationship between independent and dependent variables can be explained. Response surface plots are very helpful in learning about both the main and interaction effects of the independent variables.

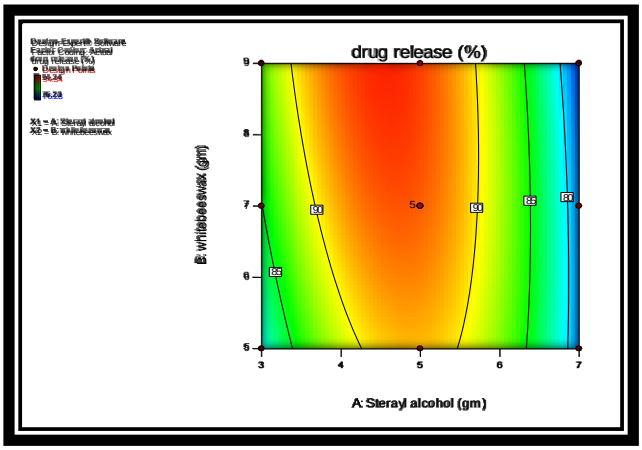


Figure 6: Contour plot showing the effect of Amount of Sterayl alcohol (X1) and Amount of Whitebees wax (X2) on response Y3

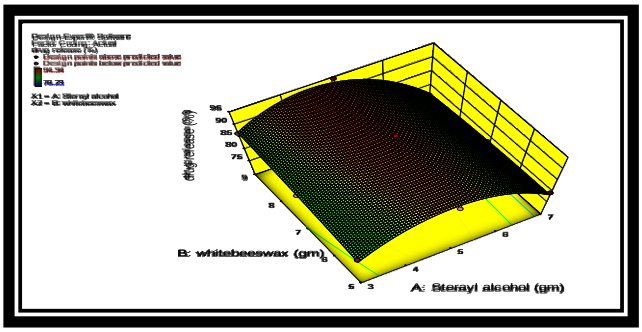


Figure 7: Response surface plot showing the effect of Amount of Sterayl alcohol (X1) and Amount of Whitebees wax (X2) on response Y3

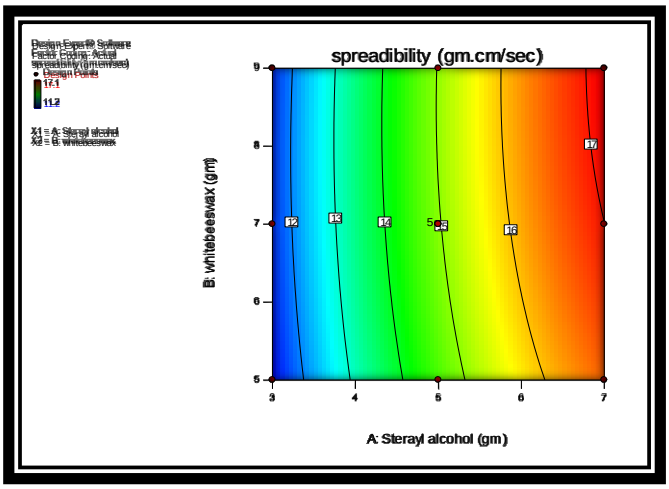


Figure 8: Contour plot showing the effect of Amount of Sterayl alcohol (X1) and Amount of Whitebees wax (X2) on response Y1

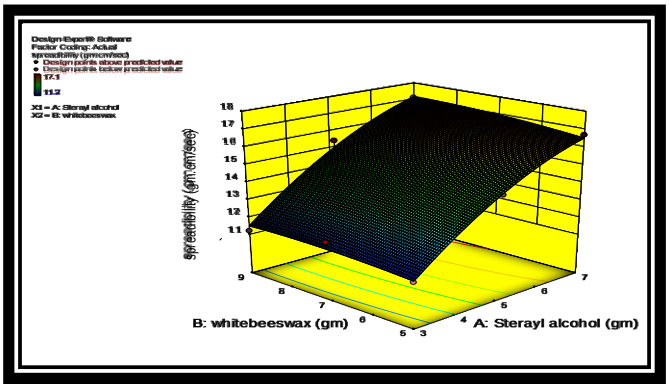


Figure 9: Response surface plot showing the effect of Amount of Sterayl alcohol (X1) and Amount of Whitebees wax (X2) on response Y1

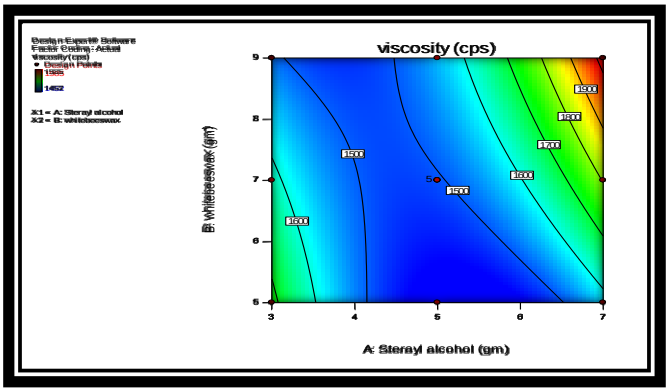


Figure 10: Contour plot showing the effect of Amount of Sterayl alcohol (X1) and Amount of Whitebees wax (X2) on response Y2

Selection of Optimized Formula

After generating the reduced model polynomial equations to relate the dependent and independent variables, the process was optimized for all three responses. Optimum formulation was selected based on the constraints set on independent variables. The final optimal experimental parameters were calculated using the extensive grid search and feasibility search provided in the Design Expert software .

Table 8: Predicted solution of optimized formula

Amount of Sterayl Alcohol (gm)	Amount of whitebees wax (gm)	Y_1	Y_2	Y_3
5.394	**8.42**	**15.56**	**1586.80**	**91.76**

Evaluation of optimized formulation

Table 9: Pre-compression and post-compression parameters of optimized formulation.

Parameters evaluated for optimized batch	Results
Spreadibility	16.75 gm*cm/sec
Viscocity	1665 cps
%drug release	98.25
Drug content	99.2
Zone of inhibition	21.02±0.10 mm after 48 hrs

In vitro drug release study

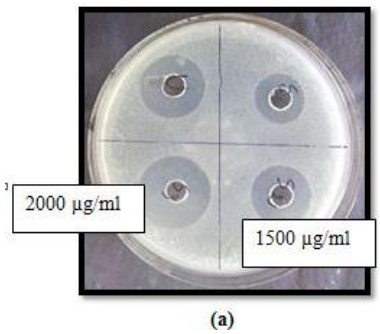
Table 10: Drug release data of optimized formulation

Time (mim)	Absorbance	Conc. (mcg/ml)	Conc. (mg/ml)	Conc.*DF	%drug release
0	0.000	0	0	0	0
15	0.192	68.3	0.068	0.068	11.79
30	0.454	151.3	0.152	0.152	25.85
60	0.732	250.3	0.250	0.250	41.65
90	0.878	306.6	0.307	0.307	53.65
120	0.090	33.0	0.033	0.033	61.44
150	0.115	41.36	0.041	0.041	74.35
180	0.129	43.25	0.043	0.043	81.23

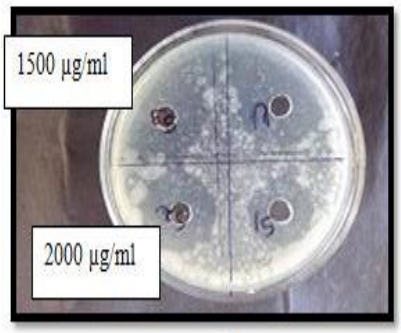
The drug release was found to be 81.23% over a time period of 180 mim

The optimized batch is compared with marketed formulation

Tetracyclin cream formulation is taken for comparison of the anti-bacterial activity at S.arueus. Herbal formulation with Termeniliabellerica is taken on another disk for the checking of zone of inhibition by disk diffusion method



(a)



(b)

Figure11 :Images of Zone of inhibition of (a)Zone of inhibition of Tetracyclin
(b) Zone of inhibition of Termenilliabellerica

Table 11: Comparison of extract and standard on S.areus

	Concentration	Zone of inhibition	
	(µg/ml)	(mean ± Standard Deviation)	
		After 24 hr	After 48 hr
Termeniliabellerica	1000	13.3±0.41	13.5±0.3
Extract	1500	16.53±0.53	15.4±0.208
	2000	20.63±0.35	22.13±0.90
Tetaracyclin	1000	15.6±0.21	16.85±0.21
	1500	18.9±0.62	19.3±0.45
	2000	21.2±0.65	23.6±0.72

Homogeneity

The formulation should be tested for homogeneity as there should not be presence of any particles. The formulation tested between the thumb and index finger didn't sowed presence of any particles and found to be homogenous.

Consistency

The test for consistency gives the information about thickness and firmness of the formulation. That may be considered important for cream to be stable for long period of time and doesn't lose its uniformity.

Observed value

Consistency of formulation: 5.3 mm.

Acid value and saponification value

Saponificationvalue is observed to be **185**

Acid Value is observed to be **0.63**

HPLC of extract

10 mg of herbal powder extract was accurately weighed containing 6-14 % of Termenillia bellerica and dissolved into 10 ml mobile phase ACN: Water (92:8) (1000 µg/ml). The solution was sonicate for 10 min and filtered through 0.45 µ whatmann filter paper. Further 0.1 ml of solution was withdrawn from above solution and diluted to 10 ml with mobile phase ACN: Water (92:8) (10 µg/ml). Parameters of obtained solution were noted at 271 nm.

Figure 12: HPLC for Standard Termenilia bellerica

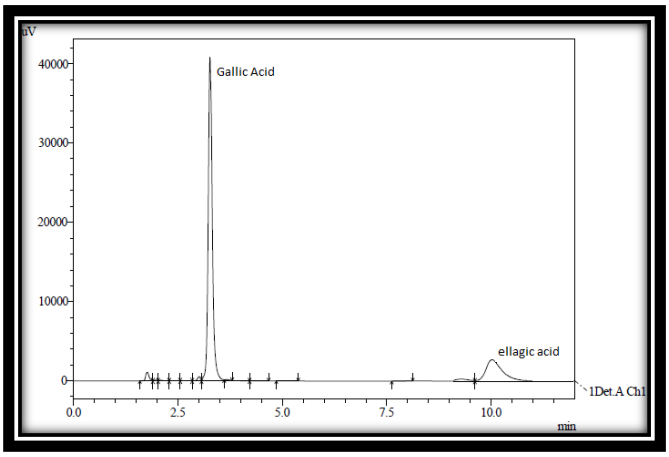


Table 12: Peak table of Biomarker

Drugs	Retention time (min)	Area	Theoretical plates	Tailing factor
Ellagic acid	10.045	79969	25963.44	1.321
Gallic acid	3.28	27476	35357.67	1.212

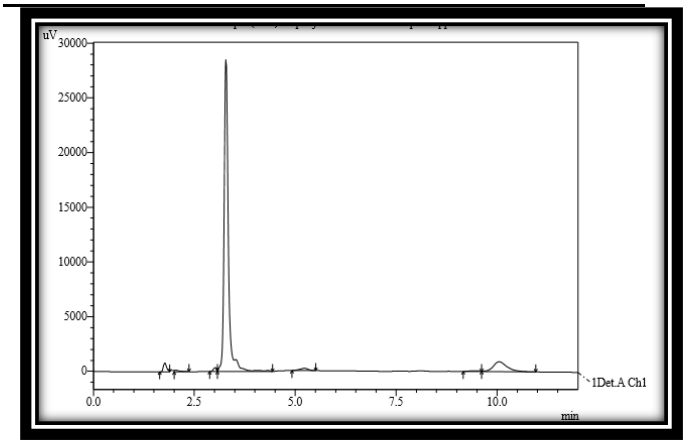


Figure 13: HPLC for extract

Table 13: Peak table of Termenilia Bellerica

Drugs	Retention time (min)	Area	Theoretical plates	Tailing factor
Ellagic acid	3.28	33101	35678.5	1.251
Gallic acid	10.045	22450	28008.19	1.288

Stability studies

Accelerated stability studies were performed for optimized formulation. The formulation was stored at

40±2°C/75±5% RH for 4 weeks. At weekly interval the samples were withdrawn and tablet evaluation tests were conducted. There was found to be no appreciable change in the drug content and in vitro drug release rate of the formulation as indicated.

Table 14:Evaluation of optimized batch after stability study

Sampling Interval days	Storage condition at 40˚C ± 2 ˚C/ 75 ± 5 % RH			
	Physical appearance	pH±SD	Viscosity±SD	Spread-ability±SD
0	Light Brown	6.02±0.035	1866.67±57.73	17.22±1.65
15	No change	6.01±0.03	1866.67±57.73	17.18±1.92
30	No change	6.01±0.02	1833.33±57.75	17.17±1.93

CONCLUSION

The present research work concludes that the The cream with Termenilia bellerica extract is showing the good anti-bacterial activityand it can be used in treating Cellulitis disease. As after the screening of plants extracts one of it is selected and it is loaded in cream formulation. Characterization of drug and individual excipients confirmed their purity. The formulation of cream is made by o/w type preparation. The Termenilia bellerica Physicochemical properties, phytoconstituents, are been find 1st to conform the extract purity. The pH, viscosity, and spreadibility is been evaluated. The 3^2 factorial designs has been made used which was helpful to optimize the final formulation with minimum trails. From the result it can be concluded that streayl alcohol and whitebees wax can be used increasing the viscosity, Spreadibility and %drug release.Further Stability studies of optimized formulation indicated that there was no significant change in physical change, pH, spreadibility and viscosity was observed for 1 month (40ºC/75% RH). Thus objective to present work of formulating the herbal cream has been achieved with success. The work can be extended by skin irritation was observed. The optimized is compared with Tetaracylin containing cream and the Zone of inhibition is seen. The Hplc of Termenilia bellericais been performed.

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